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Jessica Sandler <jessicas@peta.org> on 12/20/2002 04:08:22 PM

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cc:

Subject: Public comments on the API waxes category

Attached please find the comments of the animal protection community on the American Petroleum Institute's plan for testing waxes and related materials. We hope the API will seriously consider these concerns and suggestions.

Sincerely,

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HPV test plan comments -- wa

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December 20, 2002

Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on the API's Test Plan for the Waxes and Related
Materials Category

Dear Administrator Whitman:

The following comments on the API's High Production Volume (HPV) Challenge test plan for Waxes and Related Materials are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

The API's test plan for waxes and related substances includes eight substances from three general subcategories of slack wax, refined/finished waxes, and petrolatum. All substances in the category are actually complex mixtures of hydrocarbon compounds, with the toxicity of many of these compounds being well-characterized either as individual compounds or as part of other complex mixtures. We support the formation of a scientifically defensible category with a number of substances, as this results in fewer animals being used in the SIDS battery. However, we are very concerned about the remaining proposed testing on animals, which includes the following:

1. Combined repeat dose/reproductive/developmental study (OECD No. 422) and
2. *In vivo* mammalian erythrocyte micronucleus test (OECD No. 474 to be included at part of the repeat dose study above).

All of these tests are unnecessary. If this test plan is conducted in its present form, approximately 800 animals will be killed. Our objections are summarized immediately below:

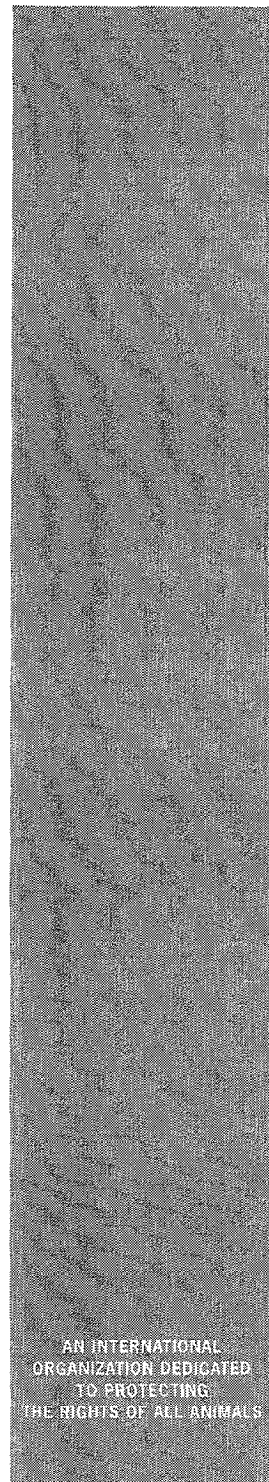
1. As acknowledged in its test plan, the API is lacking compositional data on slack waxes, specifically the spectrum of polynuclear aromatic hydrocarbons' (PNAs, also abbreviated as PAHs) content. Since PNAs are the primary identified toxic compound in this HPV test



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category, and PNA toxicity is well characterized (see below), adequate data already exist to characterize the toxicological hazard of these compounds, including slack wax, if the API were to properly characterize their analytical chemistry.

2. The category should be expanded to cover a broader range of heavy-end hydrocarbon substances.
3. The API is proposing *in vivo* genotoxicity studies on slack wax (in clear violation of the October 1999 animal protection agreement and the December 2000 *Federal Register* notice calling for the use of *in vitro* genetic toxicity testing) even though this substance has already been tested in three skin carcinogenicity studies of up to 80 weeks that all produced consistent results. These three dermal carcinogenicity studies on slack wax, while not necessarily reported in sufficient detail to fully assess subchronic effects, nonetheless indicated a weak carcinogenic potential. Several studies on the more refined waxes have already been conducted to evaluate both the subchronic and long-term effects of these substances. The results of these latter studies, when taken together are adequate to address the repeat dose toxicity of the more refined waxes.
4. The plan fails to consider the role of reduced bioavailability and solubility in the analysis.

The fundamental physical/chemical properties of these compounds include high molecular weights, low water solubility, and occurrence as solid or semi solid phases. As described on page 2 in the test plan, "the biologically available/active impurities (aromatics) are found in the oil component. At each process step, the oil and impurities content of the wax(es) is lowered. Materials similar to the oil component of the waxes are included in the Lubricating Oil Basestocks HPV Test Plan. While waxes are composed primarily on linear alkane molecules, the compounds in the Lubricating Basestocks category contain primarily branched-chain alkanes and naphthlenics." Thus, the primary toxicity associated with substances in the waxes category are present in the oil component of the materials in the waxes and related substances. The lack of toxicity of the waxes themselves is further reflected in the fact that two members of the category, paraffin waxes (8002-74-2) and petrolatum (8009-03-8), are considered Generally Recognized as Safe (GRAS) food ingredients by the Food and Drug Administration (FDA).

Since the oil components are the subject of an entirely separate category (as noted above, the Lubricating Oil Basestocks Category, which has yet to be publicly submitted to EPA for review), and the bioavailability and solubility of these oil-based toxic aromatic components would be greatly reduced due to incorporation into the waxes, it is entirely unnecessary to conduct additional testing separately on the compounds in this current (waxes) category.

Furthermore, it is unlikely that the approach proposed in this test plan will produce meaningful data, since tests are being proposed when the sponsor acknowledges that there is little specific data on the composition of the slack waxes, the proposed test material for this category. Before deciding on the need for animal testing, the more scientific approach would be to first develop more data on the composition of the proposed test material, i.e., slack wax. Once the composition has been better characterized, the complex mixtures' toxicology can then be evaluated based on the toxicities of the component chemicals of the wax. For example, abundant

information already exists on the toxicology of PNA's¹ and many other petroleum fractions,² and their many hazards. Therefore, with the combination of expanded composition information and existing toxicological information on the toxic components, an enlightened basis would be provided for evaluating toxicity of these compounds. Thus, we propose further chemical characterization and extrapolation of known toxicities on the components (which requires NO animals) versus the default to animal testing of a chemical mixture which has had inadequate chemical characterization from work in the analytical laboratory.

This approach stands in stark contrast to the proposal submitted by the API to characterize wax toxicology. It is unclear why the API would prefer to subject animals to suffering in unneeded toxicity studies when more work at the non-animal chemistry level, along with the use of the extensive toxicity data available on PNAs, would meet the demands of the HPV program. We hope that the EPA, with its stated desire to reduce the use of animals in this program, will agree with this approach and urge the API to reconsider its proposal. When a choice is available between using animals in toxicity tests versus doing more work in the chemistry lab, the EPA should encourage the API to do its chemistry homework and to spare the animals.

Furthermore, as noted above, the API admits in this test plan that the components that are likely to drive wax derivative toxicology are probably in the oil fraction of the wax mixtures. As these compounds are characterized by the Lubricating Oil Basestocks Category, it would only make sense to combine the wax category with this larger category. The EPA must encourage this more scientific and humane approach.

The API is proposing both additional *in vivo* genotoxicity and repeat dose studies, despite the fact that long term studies have been conducted to evaluate cancer potential of slack wax. These studies consistently showed some cancer potential in 80-week studies of slack wax in rodents after dermal exposure. Although these cancer studies may not fully characterize sub-chronic hazards, their results still make it clear that dermal exposure should be minimized. Additional characterization of potential toxicity from less than lifetime exposures will not provide any information that would change the obvious need to reduce exposure to these materials. Further, in that the API points to the PNA content being a controlling factor in the toxicity of these cancer studies, the subchronic and other information already available on the PNAs are more than adequate to address the toxicological concerns on all relevant endpoints under SIDS. Additional testing in animals will not provide new reasons to further reduce human exposure to these compounds nor will it result in increased protection of human health. Both the October 1999 agreement and the December 2000 *Federal Register* notice state that "as with all chemicals, before generating new information, participants should further consider whether any additional information obtained would be useful or relevant." Failure in this case to do so constitutes yet another blatant violation of minimal measures to reduce the use of animals in this program.

With regards to the proposed *in vivo* micronucleus test, the API acknowledges that "while the Testing group shares the desire to limit animal testing by using *in vitro* methodologies when possible, it decided to conduct the *in vivo* micronucleus test.[because] the physical/chemical nature of the test material precluded testing the intact material *in vitro*." This statement contradicts its stated proposal to also conduct an *in vitro* bacterial reverse mutation assay (OECD No. 471). If the Ames assay can be conducted, then no further *in vivo* testing for genotoxicity is

needed in this screening level program. This discrepancy needs to be resolved and only the *in vitro* genetic toxicity testing conducted.

Finally, this test plan does not consider any human exposure data, or the reduced bioavailability and solubility of these compounds, despite the fact that human consumption of these products is common. Any characterization of wax toxicity based on individual components would be an upper bound (or worst case) limit on toxicity since the extremely low solubility and high molecular weight makes these compounds unavailable to any animals (including humans) who might consume them. This lack of bioavailability alone should obviate the need for animal testing on the slack wax.

Unfortunately, the API's proposal for testing the waxes and related materials category suffers from the same set of problems that has characterized previous API test plans, dating as far back as its proposal to test petroleum coke. The lack of thoughtful analysis and the failure to combine testing with similar compounds has led to a gross and unnecessary use of animals in laboratory testing. We urge both the API and the EPA to seriously consider these comments and concerns and to revise the testing proposal accordingly.

We would greatly appreciate receiving a response to our concerns. I can be reached at 757-622-7382, ext.1304, or via e-mail at JessicaS@peta.org.

Sincerely,

Jessica Sandler
Federal Agency Liaison

¹ ATSDR. 1995. Toxicological Profile For Polycyclic Aromatic Hydrocarbons (PAHs). Prepared By Research Triangle Institute for the U.S. Department Of Health And Human Services. Public Health Service

² ATSDR. 1999. Toxicological Profile For Total Petroleum Hydrocarbons (TPH). Prepared by Research Triangle Institute for the U.S. Department Of Health And Human Services Public Health Service.